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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/748,131	12/27/2000	Yoko Aida	P20428.P06	3315

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EXAMINER

MYERS, CARLA J

ART UNIT	PAPER NUMBER
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1634

DATE MAILED: 11/01/2002

13

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/748,131

Applicant(s)

AIDA ET AL.

Examiner

Carla Myers

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 April 2002.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-6 and 14-20 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4, 14-18 is/are rejected.
- 7) ☒ Claim(s) 5, 6, 19 and 20 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

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1. This action is in response to Paper No. 12, filed April 1, 2002. Claims 7-13 have been canceled and claims 16-20 have been added. Accordingly, claims 1-6 and 14-20 are pending. Applicants arguments presented in the response of Paper No. 12 have been fully considered but are not persuasive to overcome all grounds of rejection. All rejections not reiterated herein are hereby withdrawn. This action is made final.
2. Claims 1-4, and 14-18 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to methods of detecting nucleic acids using primer sets wherein the primer sets are defined in terms of including a reverse primer capable of amplifying all alleles of BoLA-DRB3.2 and the forward primer is capable of amplifying all alleles in any one of two or more groups of BoLA-DRB3.2 alleles. The specification teaches a set of primers consisting of SEQ ID NO: 1-8 which hybridize to a single region within exon 2 of the BoLA-DRB3 gene and which amplify unique alleles of this gene. Accordingly, the specification has disclosed a single region of the BoLA-DRB3 gene which can be used to obtain allele and group specific primers and has adequately described forward primers consisting of SEQ ID NO: 1-8. The specification further teaches primers consisting of SEQ ID NO: 9 and 12 which amplify all alleles of BoLA-DRB3.2. However, the specification has not adequately described the broadly claimed genus of probes which are defined only in terms of their functional activity and are not defined with

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respect to their structural properties. It is noted that the claimed primers may be complementary to sequences in any other BoLA region because the primers only need to meet the limitation of being capable of amplifying all BoLA-DRB3.2 alleles or less than all BoLA-DRB3.2 alleles. It is further noted that the recitation in claims 2 and 8 that the primer comprises a portion of the DNA sequence encoding the first hypervariable region is not considered to further limit the claim because the claim does not set forth a length limitation for the "portion" and thereby the primer need only contain any, e.g., 3 nucleotides that encode any amino acid in the first hypervariable region. The specification teaches a single polymorphic region in BoLA-DRB3.2 which is useful for generating allele and group specific primers and 2 regions which can be used to generate primers which amplify all BoLA-DRB3.2 alleles. *Vas-Cath Inc. V. Mahurkar*, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed". Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision. In *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling

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within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA... requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention". In analyzing whether the written description requirement is met for a genus claim, it is first determined whether a representative number of species have been described by their complete structure. In the instant case, only 8 members of the broadly claimed genus of forward primers and 2 members of the broadly claimed genus of primers that amplify all BoLA-DRB3.2. alleles have been defined by their structure. It is then determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics. In the instant case, no such identifying characteristics have been provided for any of the claimed primers. While at the time of filing applicants were in possession of primers consisting of SEQ ID NO: 1-9 and 12, the limited information provided in the specification is not deemed sufficient to reasonably convey to one of skill in the art that Applicants were in possession of a representative number of the claimed BoLA primers and thus the written description requirement has not been satisfied for the claims as they are broadly written. Applicants attention is drawn to the Guidelines for the Examination of Patent Applications under 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

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RESPONSE TO ARGUMENTS:

In the response of Paper No. 12, Applicants traverse this rejection by arguing that once a hypervariable region has been identified, one of skill in the art can make additional primers to this region. It is further stated that the disclosure of 8 primers is considered to be representative of the complete genus of primers which amplify all alleles in any one of two or more groups of alleles of BoLA-DRB3.2.

Applicants arguments have been fully considered but are not persuasive to overcome the present grounds of rejection. The claims are not limited to primers which amplify any particular allelic variants of the BoLA-DRB3.2 region. Rather, the claims include primers which specifically amplify allelic variants which are not characterized in the specification and/or which have not yet been characterized in the art. The specification has identified only one region within exon 2 which is highly variable and the claims are not limited to primers which specifically amplify the allelic variants of this known variable region. While it is routine in the art to generate primers to a known allele (i.e., to an allele which has been characterized with respect to its polymorphic sequence and with respect to its flanking sequences), it is not routine in the art to identify novel alleles and then generate primers to these alleles. Additionally, 2 regions have been identified which amplify all alleles of BoLA-DRB3.2. The specification does not characterize any additional regions which are highly conserved and from which additional primers can be obtained. While the specification has identified 8 primers which amplify alleles from 2 or more groups of the alleles of BoLA-DRB3.2, it is expected that the genus of primers

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which amplify additional allelic variants is significantly larger than 8. In the absence of evidence to the contrary, 8 is not considered to be representative of the claimed genus of primers which amplify all alleles in 2 or more groups of alleles of BoLA-DRB3.2. Additionally, the identification of 2 primers which amplify all alleles of BoLA-DRB3.2 is not considered to be representative of the genus of all possible primers which amplify all alleles of BoLA-DRB3.2, wherein the primers may comprise any unspecified sequence and may anneal to any unspecified region of bovine genomic DNA.

4. Claims 3-4, and 17-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 3-4 and 17-18 and newly are indefinite over the recitation of "alleles of BoLA-DRB3.2 are classified into the two or more groups of alleles" and "are classified into 8 groups" because it is not clear as to how these phrases are intended to further limit the claims. It is unclear as to how the step of classifying the alleles further defines the claimed primer set.

RESPONSE TO ARGUMENTS:

In the response of Paper No. 12, Applicants state that the claims as written makes clear that the groups are comprised of the 96 alleles. However, it remains unclear as to how the phrase "are classified" further limits the claims. While the claims have been amended to recite methods, rather than products (primers), the recitations of "are classified" relate to the primers and not to

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the methods. It is unclear as to whether the claims include an additional step of classifying the alleles into the stated groups or whether the claims intend to further limit the properties of the primers themselves (e.g., to indicate that the primers amplify 2 or more groups out of 96 possible alleles of BoLA-DRB3.2).

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(c) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 1-4, 14 and 16-18 are rejected under 35 U.S.C. 102(b) as being anticipated by Ellegren et al (Animal Genetics (1993) 24: 269-275).

Ellegren et al teaches allele-specific primers which hybridize to unique sequences in the BoLA-DRB3.2 gene (page 270). These oligonucleotide primers are considered to be capable of amplifying all alleles in one of two or more groups since the 5 oligonucleotides amplify distinct BoLA-DRB3.2 alleles. It is noted that the claims and specification do not define particular groups, and thereby the alleles may be divided by any criteria into groups. Thus, the oligonucleotide primers are each considered to be capable of amplifying alleles of one group and not alleles of any of the remaining 7 groups. The oligonucleotides are also considered to comprise a portion of a DNA sequence encoding an amino acid sequence of the first

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hypervariable region of BoLA-DRB3.2 since the oligonucleotides comprise at least one nucleotide of the same identity as a nucleotide in the stated DNA sequence. Furthermore, Ellegren teaches performing PCR using one of the allele-specific primers together with the LA31 primer. In the absence of evidence to the contrary, the general LA31 primer is considered to be a primer which is capable of amplifying all BoLA-DRB3.2 alleles. Ellegren further teaches sequencing the amplified DRB3.2 alleles (see page 272).

RESPONSE TO ARGUMENTS:

In the response of Paper No. 12, Applicants traverse this rejection by stating that the PCR primers of Ellegren amplify at least 2 different DRB3 alleles "as noted by the '+' in the columns." Thereby, Applicants conclude that Ellegren does not teach the claimed methods. This argument is not convincing because the claims include methods which utilize primers which amplify more than one DRB3 allele. The claims require only that the primers amplify all alleles in any one of two or more alleles of BoLA-DRB3.2. What constitutes a group is not defined in the claims or in the specification. Thereby, a group may be any 2 or more alleles of BoLA-DRB3.2, as long as the group does not contain all BoLA-DRB3.2 alleles. The primers of Ellegren meet each of the claim limitations because the primers of Ellegren amplify less than all of the possible BoLA-DRB3.2 alleles.

6. Claims 5, 6, 19 and 20 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

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THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carla Myers whose telephone number is (703) 308-2199. The examiner can normally be reached on Monday-Thursday from 6:30 AM-5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703)-308-1152. The fax number for the Technology Center is (703)-305-3014 or (703)-305-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the receptionist whose telephone number is (703) 308-0196.

Carla Myers

October 29, 2002

Carla Myers
CARLA J. MYERS
PRIMARY EXAMINER